4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0800]

Guidance for Industry on Regulatory Classification of Pharmaceutical Co-Crystals; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled "Regulatory Classification of Pharmaceutical Co-Crystals." This guidance provides applicants of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) with the Center for Drug Evaluation and Research's (CDER's) current thinking on the appropriate regulatory classification of pharmaceutical co-crystal solid-state forms. This guidance also provides information about the data the applicant should submit to support the appropriate classification of a co-crystal, as well as the regulatory implications of the classification.

The recommendations in this guidance apply to materials that the Agency has not previously evaluated and determined to be pharmaceutical co-crystals. The recommendations do not apply to materials that the Agency has previously designated as salts, complexes, or other non-co-crystalline forms.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one self-

addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Regulatory Classification of Pharmaceutical Co-Crystals." This guidance provides applicants of NDAs and ANDAs with CDER's current thinking on the appropriate regulatory classification of pharmaceutical co-crystal solid-state forms. This guidance also provides information about the data the applicant should submit to support the appropriate classification of a co-crystal, as well as the regulatory implications of the classification.

On December 2, 2011 (76 FR 75551), FDA announced the availability of the draft version of this guidance. The public comment period closed on March 1, 2012. A number of comments were received from the public, all of which the Agency considered carefully as it finalized the guidance and made appropriate changes. Any changes to the guidance were minor and made to clarify statements in the draft guidance.

Co-crystals are solids that are crystalline materials composed of two or more molecules in the same crystal lattice. These solid-state forms, composed of an active pharmaceutical ingredient (API) with a neutral guest compound (also referred to as a conformer), have been the focus of significant interest in drug product development. Pharmaceutical co-crystals have opened the opportunity for engineering solid-state forms designed to have tailored properties to enhance drug product bioavailability and stability, as well as enhance processability of the solid material inputs in drug product manufacture. Pharmaceutical co-crystals are of interest because they offer the advantage of generating a diverse array of solid-state forms from APIs that lack ionizable functional groups needed for salt formation.

Traditionally, solid-state polymorphic forms of an API are classified as either crystalline, amorphous, or solvate and hydrate forms, and applicable regulatory schemes for these solid-state polymorphic forms are well-defined. Co-crystals, however, are distinguishable from these traditional pharmaceutical solid-state forms. Unlike polymorphs, which generally speaking contain only the API within the crystal lattice, co-crystals are composed of an API with a neutral guest compound in the crystal lattice. Similarly, unlike salts, where the components in the crystal lattice are in an ionized state, a co-crystal's components are in a neutral state and interact via nonionic interactions.

At present, no formal regulatory policy exists governing the classification of pharmaceutical co-crystals. In response to this need for regulatory guidance, the guidance provides the Agency's current thinking on the appropriate classification of co-crystal solid-state forms.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on regulatory classification of pharmaceutical co-crystals. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either written comments regarding this document to the Division of Dockets Management (see ADDRESSES) or electronic comments to http://www.regulations.gov. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received

comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

III. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. This guidance refers to information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR 314.50(d)(1) and 314.94(a)(5) and 314.94(a)(9) have been approved under OMB control number 0910–0001. The collections of information in the current good manufacturing practice (CGMP) regulations (21 CFR part 211) have been approved under OMB control number 0910-0139.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: April 22, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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